

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (original): A therapeutic or diagnostic composition comprising particles of a polymer matrix into which is absorbed aqueous liquid, the particles having diameters in the range 40 to 4000 μm , characterised in that surfaces of the particles express zwitterionic groups.

2. (original): A composition according to claim 1 in which the polymer matrix is substantially non-biodegradable.

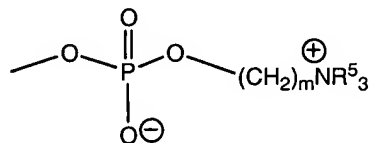
3. (original): A composition according to claim 1 or claim 2 which comprises a continuous aqueous medium in an amount sufficient to suspend the particles.

Claims 4-33. (canceled).

34. (new): A composition according to claim 1 which is sterile.

35. (new): A composition according to claim 1 in which the zwitterionic group is ammonium, phosphonium, or sulphonium phosphate or phosphonate ester zwitterionic group.

36. (new): A composition according to claim 5 in which the zwitterionic group has general formula III



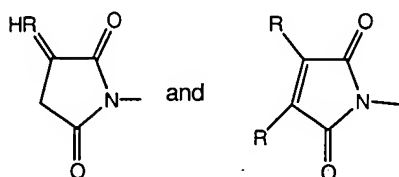
III

where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4.

37. (new): A composition according to claim 1 in which the zwitterionic groups are pendant groups on a polymer formed from ethylenically unsaturated monomers including a monomer of the general formula I



in which Y is an ethylenically unsaturated group selected from the group consisting of $H_2C=CR-CO-A-$, $H_2C=CR-C_6H_4-A^1-$, $H_2C=CR-CH_2A^2$, $R^2O-CO-CR=CR-CO-O$, $RCH=CH-CO-O-$, $RCH=C(COOR^2)CH_2-CO-O$,



A is $-O-$ or NR^1 ;

A^1 is selected from the group consisting of a bond, $(CH_2)_lA^2$ and $(CH_2)_lSO_3-$ in which l is 1 to 12;

A^2 is selected from the group consisting of a bond, $-O-$, $O-CO-$, $CO-O$, $CO-NR^1-$, $-NR^1-CO$, $O-CO-NR^1-$, $NR^1-CO-O-$;

R is hydrogen or C_{1-4} alkyl;

R^1 is hydrogen, C_{1-4} alkyl or BX ;

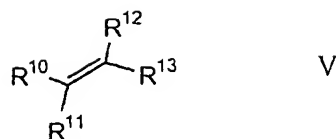
R^2 is hydrogen or C_{1-4} alkyl;

B is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxalkylene) group, optionally containing one or more fluorine substituents;

X is the zwitterionic group.

38. (new): A composition according to claim 37 in which Y is $H_2C=CR-CO-A$.

39. (new): A composition according to claim 37 in which the ethylenically unsaturated monomers further comprise comonomers of the general formula V



in which R^{10} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{14}$ in which R^{14} is selected from the group consisting of hydrogen and C_{1-4} alkyl;

R^{11} is selected from the group consisting of hydrogen, halogen and C_{1-4} alkyl;

R^{12} is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl and groups $COOR^{14}$ provided that R^{10} and R^{12} are not both $COOR^{14}$; and

R^{13} is selected from the group consisting of C_{1-10} alkyl, C_{1-20} alkoxy carbonyl, mono-or di- (C_{1-20} alkyl) amino carbonyl, C_{6-20} aryl, C_{7-20} aralkyl, C_{6-20} aryloxy carbonyl, C_{1-20} - aralkyloxy carbonyl, C_{6-20} arylamino carbonyl, C_{7-20} aralkyl-amino, hydroxyl and C_{2-10} acyloxy groups, any of which may have one or more substituents selected from the group consisting of halogen atoms, alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amino (including mono and di-alkyl amino and trialkylammonium in which the alkyl groups may be substituted), carboxyl, sulphonyl, phosphoryl, phosphino (including mono- and di- alkyl phosphine and tri-alkylphosphonium), zwitterionic, hydroxyl, vinyloxy carbonyl and other vinylic and allylic substituents, and reactive silyl and silyloxy groups;

or R^{13} and R^{12} or R^{13} and R^{11} may together form $-CONR^{15}CO$ in which R^{15} is a C_{1-20} alkyl group.

40. (new): A composition according to claim 39 in which the comonomer is a non-ionic comonomer.

41. A composition according to claim 1 in which the matrix polymer is a polyion complex.

42. A composition according to claim 1 in which the polymer matrix is covalently crosslinked.

43. A composition according to claim 42 in which the matrix polymer is formed from ethylenically unsaturated monomers including a di- or higher-valent ethylenically unsaturated monomer.

44. A composition according to claim 42 in which covalent crosslinking has been carried out by reaction of functional groups on preformed polymer subjected to conditions whereby intermolecular reaction takes place to form covalent bonds.

45. A composition according to claim 1 in which the matrix polymer is based on polyvinylalcohol.

46. A composition according to claim 45 in which the polyvinyl alcohol is crosslinked by reaction of pendant ethylenically unsaturated crosslinking groups by radical polymerisation.

47. A composition according to claim 1 in which the particles, when imbibed with physiological saline at room have a water content of at least 30% by weight.

48. A composition according to claim 1 in which the particles are substantially spherical.

49. A composition according to claim 1, in which the diameters of the particles, when fully imbibed with water, are in the range 150 μm to 3000 μm .

50. A composition according to claim 1 which is stable on storage at room temperature such that the particles do not coalesce to the extent that they cannot be redispersed upon gentle agitation.

51. Method of treatment of an animal in which a composition according to claim 1 is administered to an animal for therapy or diagnosis.

52. Method according to claim 51 in which the composition is administered to form an embolus.

53. Method according to claim 52 in which the composition is administered for uterine fibroid embolisation, embolisation of vessels around tumours or tumour-excision sites, embolisation of varicose veins or varicoceles, embolisation of arteriovenous malformations or

venous malformations, hemostasis of gastro-intestinal bleeds, embolisation of fistulas or embolisation of fallopian tubes, or seminiferous tubes for sterilisation purposes.

54. Microspheres comprising a core which is a matrix of a water-insoluble water-absorbing polymer, which when imbibed with physiological saline at equilibrium at room temperature have diameters in the range 40 to 4000 μm , characterised by expressing zwitterions over their external surfaces.

55. Microspheres according to claim 54, which when fully imbibed with physiological saline have a water content of at least 30% by weight.

56. A kit comprising, each in separate vessels, a plurality of populations of microspheres according to claim 54 or 55, the populations differing in respect of the range of particle diameters.

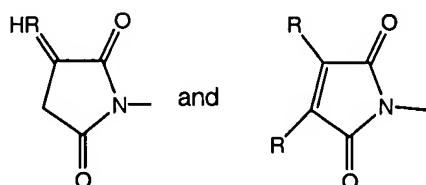
57. A kit according to claim 56 in which the size range of each of the populations of microspheres, when imbibed with physiological saline to equilibrium at room temperature, is 50 to 1000 μm , preferably 150 to 300 μm .

58. A kit according to claim 57 in which the diameters of the different populations substantially do not overlap with one another.

59. A process of inverse suspension polymerisation in which ethylenically unsaturated monomers including a zwitterionic monomer of the general formula I



in which Y is an ethylenically unsaturated group selected from the group consisting of $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$, $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4-\text{A}^1-$, $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$, $\text{R}^2\text{O}-\text{CO}-\text{CR}=\text{CR}-\text{CO}-\text{O}$, $\text{RCH}=\text{CH}-\text{CO}-\text{O}-$, $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$,



A is -O- or NR^1 ;

A^1 is selected from the group consisting of a bond, $(\text{CH}_2)_l \text{A}^2$ and $(\text{CH}_2)_l \text{SO}_3^-$ in which l is 1 to 12;

A^2 is selected from the group consisting of a bond, -O-, O-CO-, CO-O, CO- NR^1 -, - NR^1 -CO, O-CO- NR^1 -, NR^1 -CO-O-;

R is hydrogen or C_{1-4} alkyl;

R^1 is hydrogen, C_{1-4} alkyl or BX;

R^2 is hydrogen or C_{1-4} alkyl;

B is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxalkylene) group, optionally containing one or more fluorine substituents; and

X is the zwitterionic group

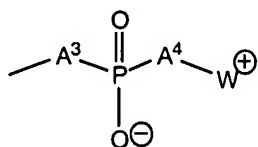
and miscible comonomers, as a liquid monomer mixture, are dispersed into a continuous liquid non-solvent to form a dispersed phase, and initiator is added to initiate radical polymerisation in the dispersed phase, and the particles of polymer formed from the dispersed phase are recovered.

60. A process according to claim 59 in which the ethylenically unsaturated monomers include di- or higher functional crosslinking monomer.

61. A process according to claim 59 or claim 60 in which the monomer mixture comprises water.

62. A process according to claim 59 in which the liquid non-solvent comprises a water-in-oil stabiliser prior to addition of the monomer mixture.

63. A composition according to claim 35 in which the zwitterionic group is a group of the general formula II



II

in which the moieties A^3 and A^4 , which are the same or different, are -O-, -S-, -NH- or a valence bond, and W^+ is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is a C_{1-12} -alkanediyl group,

64. A composition according to claim 63 in which W^+ is a group of formula $-W^1-N^+R^3_3$, $-W^1-P^+R^4_3$, $-W^1-S^+R^4_2$ or $-W^1-Het^+$ in which:

W^1 is alkanediyl of 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, or alkylene aryl alkylene, cycloalkanediyl, alkylene cycloalkyl, cycloalkyl alkylene or alkylene cycloalkyl alkylene, which group W^1 optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R^3 are the same or different and each is hydrogen or alkyl of 1 to 4 carbon atoms, or aryl, or two of the groups R^3 together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R^3 together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R^3 is substituted by a hydrophilic functional group, and

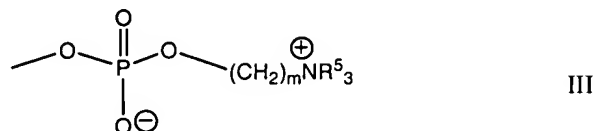
the groups R^4 are the same or different and each is R^3 or a group OR^3 , where R^3 is as defined above; or

Het is an aromatic nitrogen-, phosphorus- or sulphur-, containing ring.

65. A composition according to claim 40 in which the nonionic comonomer is selected from the group consisting of C_{1-24} alkyl(alk)-acrylates and -acrylamides, mono-, and di-hydroxy- C_{1-6} -alkyl(alk)-acrylates, and -acrylamides, oligo(C_{2-3} alkoxy) C_{2-18} -alkyl (alk)-acrylates, -acrylamides, acrylamide, styrene, vinylacetate and N-vinylactams.

66. A therapeutic or diagnostic composition comprising particles of a polymer matrix into which is absorbed aqueous liquid, the particles having diameters in the range 40 to 4000 μm ,

characterised in that surfaces of the particles express zwitterionic groups having general formula III

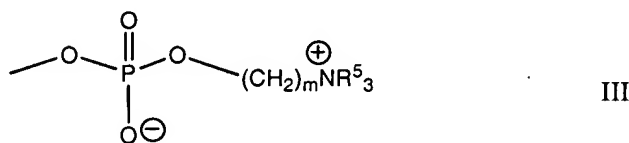


where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4,

in which the matrix polymer is based on polyvinyl alcohol and the particles are substantially spherical.

67. A composition according to claim 66 in which the particles have diameters in the range 150 to 2000 μm when fully imbibed with water.

68. Microspheres according to claim 54 in which the zwitterions have general formula III



where the groups R^5 are the same or different and each is hydrogen or C_{1-4} alkyl, and m is from 1 to 4.

69. Microspheres according to claim 54 in which the polymer is based on polyvinyl alcohol.